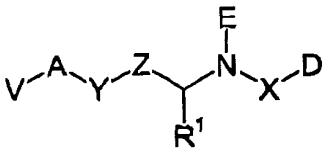
ALLOWED CLAIMS (5576.200)

(1, 5, 13, 16-18, 22, 23, 30, 43-46, 49, 51, 53, 55-57, 59, 63, 68-71, 87-90 and 92-118)

1. A compound of formula (I):

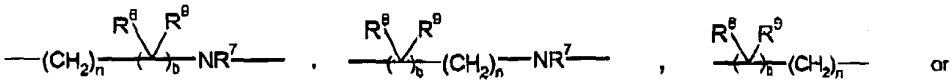


(I)

wherein

V is -COOH

A is



or

$-NR^7CH_2-$,

wherein

b is 0 or 1,

n is 0, 1, 2 or 3,

R^7 is hydrogen, C_{1-6}-alkyl or C_{3-6}-cycloalkyl-C_{1-6}-alkyl,

R^8 and R^9 independently are hydrogen or C_{1-6}-alkyl,

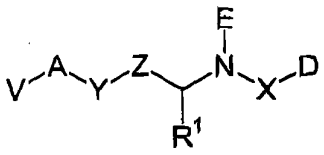
Y is -C(O)-,

Z is

ALLOWED CLAIMS IN US SERIAL NO. 09/572,553

(1, 5, 13, 16-18, 22, 23, 30, 43-46, 49, 51, 53, 55-57, 59, 63, 68-71, 87-90 and 92-118)

1. A compound of formula (I):

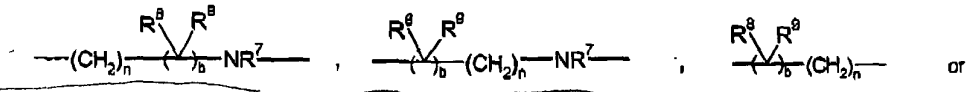


(I)

wherein

V is -COOH

A is



-NR^7CH_2-,

wherein

b is 0 or 1,

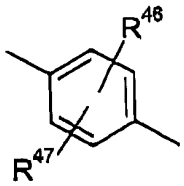
n is 0, 1, 2 or 3,

R^7 is hydrogen, C_{1-6}-alkyl or C_{3-8}-cycloalkyl-C_{1-6}-alkyl,

R^8 and R^9 independently are hydrogen or C_{1-6}-alkyl,

Y is -C(O)-,

Z is

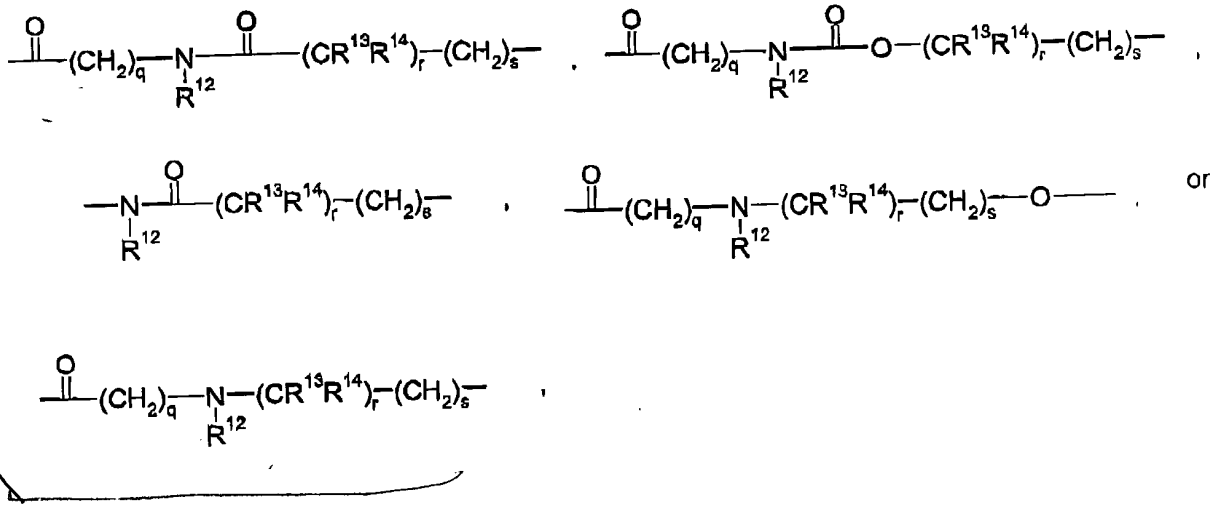


wherein R^{46} and R^{47} independently are selected from hydrogen, halogen, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, $-OR^{10}$, $-NR^{10}R^{11}$ and C_{1-6}-alkyl,

wherein R^{10} and R^{11} independently are hydrogen or C_{1-6}-alkyl,

R^1 is hydrogen or C_{1-6}-alkyl,

X is



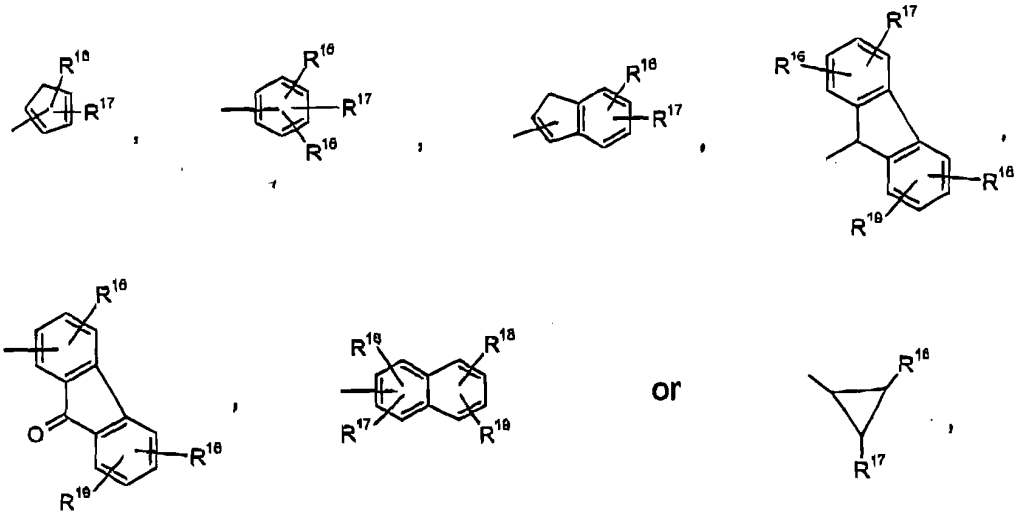
wherein

r is 0 or 1,

q and s independently are 0, 1, 2 or 3,

R^{12}, R^{13}, and R^{14} independently are hydrogen or C_{1-6}-alkyl,

D is



wherein

R^{16}, R^{17}, R^{18} and R^{19} independently are

- hydrogen, halogen, -CN, $-CH_2CN$, $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-OS(O)_2CF_3$, $-SCF_3$, $-NO_2$, $-OR^{21}$, $-NR^{21}R^{22}$, $-SR^{21}$, $-NR^{21}S(O)_2R^{22}$, $-S(O)_2NR^{21}R^{22}$, $-S(O)NR^{21}R^{22}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-OS(O)_2R^{21}$, $-C(O)NR^{21}R^{22}$, $-OC(O)NR^{21}R^{22}$, $-NR^{21}C(O)R^{22}$, $-CH_2C(O)NR^{21}R^{22}$, $-OCH_2C(O)NR^{21}R^{22}$, $-CH_2OR^{21}$, $-CH_2NR^{21}R^{22}$, $-OC(O)R^{21}$, $-C(O)R^{21}$ or $-C(O)OR^{21}$,

- C_{1-6}-alkyl, C_{2-6}-alkenyl or C_{2-6}-alkynyl,

  optionally substituted with one or more substituents selected from $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-SCF_3$, $-OR^{21}$, $-NR^{21}R^{22}$, $-SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-C(O)NR^{21}R^{22}$, $-OC(O)NR^{21}R^{22}$, $-NR^{21}C(O)R^{22}$, $-OCH_2C(O)NR^{21}R^{22}$, $-C(O)R^{21}$ and $-C(O)OR^{21}$,

- C_{3-8}-cycloalkyl, C_{4-8}-cycloalkenyl, heterocyclyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkoxy, C_{3-8}-cycloalkyloxy, C_{3-8}-cycloalkyl-C_{1-6}-alkylthio, C_{3-8}-cycloalkylthio, C_{3-8}-cycloalkyl-C_{2-6}-alkenyl, C_{3-8}-cycloalkyl-C_{2-6}-alkynyl, C_{4-8}-cycloalkenyl-C_{1-6}-alkyl, C_{4-}

$_{6}$-cycloalkenyl-C_{2-6}-alkenyl, C_{4-6}-cycloalkenyl-C_{2-6}-alkynyl, heterocyclyl-C_{1-6}-alkyl, heterocyclyl-C_{2-6}-alkenyl or heterocyclyl-C_{2-6}-alkynyl,

of which the cyclic moieties optionally are substituted with one or more substituents selected from

$-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-SCF_3$, $-OR^{21}$, $-NR^{21}R^{22}$, $-SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-C(O)NR^{21}R^{22}$, $-OC(O)NR^{21}R^{22}$, $-NR^{21}C(O)R^{22}$, $-OCH_2C(O)NR^{21}R^{22}$, $-C(O)R^{21}$ and $-C(O)OR^{21}$,

C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl,

optionally substituted with one or more substituents selected from $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-SCF_3$, $-OR^{21}$, $-NR^{21}R^{22}$, $-SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-C(O)NR^{21}R^{22}$, $-OC(O)NR^{21}R^{22}$, $-NR^{21}C(O)R^{22}$, $-OCH_2C(O)NR^{21}R^{22}$, $-C(O)R^{21}$ and $-C(O)OR^{21}$,

- aryl, aryloxy, aryloxycarbonyl, aroyl, aryl-C_{1-6}-alkoxy, aryl-C_{1-6}-alkyl, aryl-C_{2-6}-alkenyl, aryl-C_{2-6}-alkynyl, heteroaryl, heteroaryl-C_{1-6}-alkyl, heteroaryl-C_{2-6}-alkenyl or heteroaryl-C_{2-6}-alkynyl,

  of which the aryl and heteroaryl moieties optionally are substituted with one or more substituents selected from

  halogen, $-CN$, $-CH_2CN$, $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-OS(O)_2CF_3$, $-SCF_3$, $-NO_2$, $-OR^{21}$, $-NR^{21}R^{22}$, $-SR^{21}$, $-NR^{21}S(O)_2R^{22}$, $-S(O)_2NR^{21}R^{22}$, $-S(O)NR^{21}R^{22}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-OS(O)_2R^{21}$, $-C(O)NR^{21}R^{22}$, $-OC(O)NR^{21}R^{22}$, $-NR^{21}C(O)R^{22}$, $-CH_2C(O)NR^{21}R^{22}$, $-OCH_2C(O)NR^{21}R^{22}$, $-CH_2OR^{21}$, $-CH_2NR^{21}R^{22}$, $-OC(O)R^{21}$, $-C(O)R^{21}$ and $-C(O)OR^{21}$,

  C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl,

optionally substituted with one or more substituents selected from $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-SCF_3$, $-OR^{21}$, $-NR^{21}R^{22}$, $-SR^{21}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-C(O)NR^{21}R^{22}$, $-OC(O)NR^{21}R^{22}$, $-NR^{21}C(O)R^{22}$, $-OCH_2C(O)NR^{21}R^{22}$, $-C(O)R^{21}$ and $-C(O)OR^{21}$,

wherein R^{21} and R^{22} independently are hydrogen, $-CF_3$, C_{1-6}-alkyl, tri-C_{1-6}-alkylsilyl, C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl-C_{1-6}-alkyl, aryl, aryl-C_{1-6}-alkyl or heteroaryl,

or R^{21} and R^{22} when attached to the same nitrogen atom together form a 3 to 8 membered heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulfur, and optionally containing one or two double bonds,

or two of the groups R^{16} to R^{19} when placed in adjacent positions together form a bridge $-(CR^{16'}R^{17'})_a-O-(CR^{18'}R^{19'})_c-O-$,

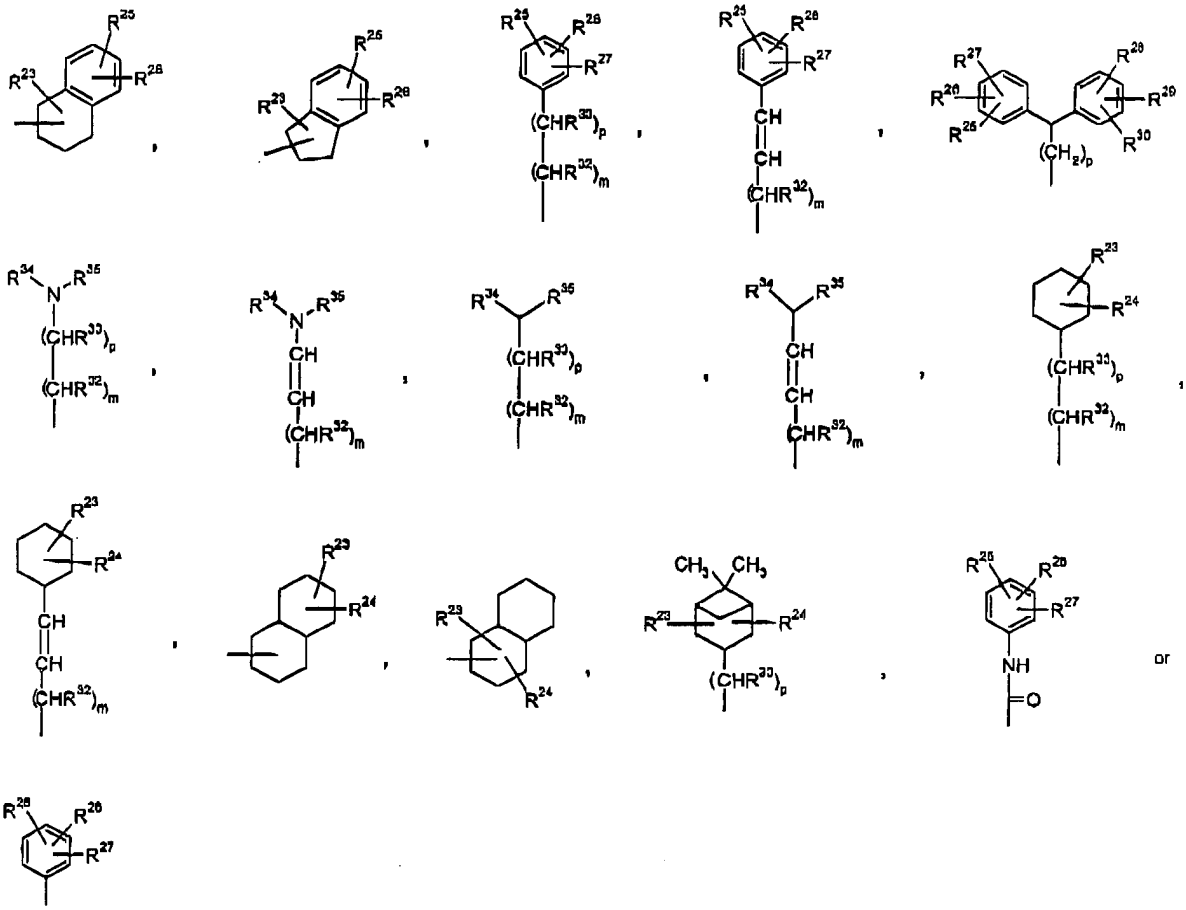
wherein

a is 0, 1 or 2,

c is 1 or 2,

$R^{16'}$, $R^{17'}$, $R^{18'}$ and $R^{19'}$ independently are hydrogen, C_{1-6}-alkyl or halogen,

E is a 3 to 9 membered mono- or bicyclic ring optionally containing one or two double bonds wherein one or two groups R^{23} and R^{24} are attached to the same or different ring carbon atoms or



wherein

m and p independently are 0, 1, 2, 3 or 4, with the proviso that when both m and p are present in the same formula at least one of m and p is different from 0,

R^{23} and R^{24} independently are

- hydrogen, -CHF_2, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2CF_3, -OCF_2CHF_2, -SCF_3, -OR^{36}, -$NR^{36}R^{37}$, -SR^{36}, -$S(O)R^{36}$, -$S(O)_2R^{36}$, -$C(O)NR^{36}R^{37}$, -$OC(O)NR^{36}R^{37}$, -$NR^{36}C(O)R^{37}$, -$OCH_2C(O)NR^{36}R^{37}$, -$C(O)R^{36}$ or -$C(O)OR^{36}$,

- C_{1-6}-alkyl, C_{2-6}-alkenyl or C_{2-6}-alkynyl,

optionally substituted with one or more substituents selected from -CHF_2, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2CF_3, -OCF_2CHF_2, -SCF_3, -OR^{36}, -$NR^{36}R^{37}$, -SR^{36}, -$S(O)R^{36}$, -$S(O)_2R^{36}$, -$C(O)NR^{36}R^{37}$, -$OC(O)NR^{36}R^{37}$, -$NR^{36}C(O)R^{37}$, -$OCH_2C(O)NR^{36}R^{37}$, -$C(O)R^{36}$ and -$C(O)OR^{36}$,

- C_{3-8}-cycloalkyl, C_{3-8}-cycloalkylidene, C_{4-8}-cycloalkenyl, heterocyclyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl, C_{3-8}-cycloalkyl-C_{2-6}-alkenyl, C_{3-8}-cycloalkyl-C_{2-6}-alkynyl, C_{4-8}-cycloalkenyl-C_{1-6}-alkyl, C_{4-8}-cycloalkenyl-C_{2-6}-alkenyl, C_{4-8}-cycloalkenyl-C_{2-6}-alkynyl, heterocyclyl-C_{1-6}-alkyl, heterocyclyl-C_{2-6}-alkenyl or heterocyclyl-C_{2-6}-alkynyl,

  of which the cyclic moieties optionally are substituted with one or more substituents selected from

  -CHF_2, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2CF_3, -OCF_2CHF_2, -SCF_3, -OR^{36}, -$NR^{36}R^{37}$, -SR^{36}, -$S(O)R^{36}$, -$S(O)_2R^{36}$, -$C(O)NR^{36}R^{37}$, -$OC(O)NR^{36}R^{37}$, -$NR^{36}C(O)R^{37}$, -$OCH_2C(O)NR^{36}R^{37}$, -$C(O)R^{36}$ and -$C(O)OR^{36}$,

  C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl,

  optionally substituted with one or more substituents selected from -CHF_2, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2CF_3, -OCF_2CHF_2, -SCF_3, -OR^{36}, -$NR^{36}R^{37}$, -SR^{36}, -$S(O)R^{36}$, -$S(O)_2R^{36}$, -$C(O)NR^{36}R^{37}$, -$OC(O)NR^{36}R^{37}$, -$NR^{36}C(O)R^{37}$, -$OCH_2C(O)NR^{36}R^{37}$, -$C(O)R^{36}$ and -$C(O)OR^{36}$,

- aryl, aryloxy, aroyl, aryl-C_{1-6}-alkoxy, aryl-C_{1-6}-alkyl, aryl-C_{2-6}-alkenyl, aryl-C_{2-6}-alkynyl, heteroaryl, heteroaryl-C_{1-6}-alkyl, heteroaryl-C_{2-6}-alkenyl or heteroaryl-C_{2-6}-alkynyl,

  of which the aryl and heteroaryl moieties optionally are substituted with one or more substituents selected from

  halogen, -CN, -CH_2CN, -CHF_2, -CF_3, -OCF_3, -$OCHF_2$, -OCH_2CF_3, -OCF_2CHF_2, -$OS(O)_2CF_3$, -SCF_3, -NO_2, -OR^{36}, -$NR^{36}R^{37}$, -SR^{36}, -$NR^{36}S(O)_2R^{37}$, -$S(O)_2NR^{36}R^{37}$, -$S(O)NR^{36}R^{37}$, -$S(O)R^{36}$, -$S(O)_2R^{36}$,

$-OS(O)_2R^{36}$, $-C(O)NR^{36}R^{37}$, $-OC(O)NR^{36}R^{37}$, $-NR^{36}C(O)R^{37}$, $-CH_2C(O)NR^{36}R^{37}$, $-CH_2C(O)NR^{36}R^{37}$, $-CH_2OR^{36}$, $-CH_2NR^{36}R^{37}$, $-OC(O)R^{36}$, $-C(O)R^{36}$ and $-C(O)OR^{36}$,

C_{1-6}-alkyl, C_{2-6}-alkenyl and C_{2-6}-alkynyl,

optionally substituted with one or more substituents selected from $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, $-OCH_2CF_3$, $-OCF_2CHF_2$, $-SCF_3$, $-OR^{36}$, $-NR^{36}R^{37}$, $-SR^{36}$, $-S(O)R^{36}$, $-S(O)_2R^{36}$, $-C(O)NR^{36}R^{37}$, $-OC(O)NR^{36}R^{37}$, $-NR^{36}C(O)R^{37}$, $-OCH_2C(O)NR^{36}R^{37}$, $-C(O)R^{36}$ and $-C(O)OR^{36}$,

wherein R^{36} and R^{37} independently are hydrogen, C_{1-6}-alkyl or aryl,

of which the aryl moiety optionally is substituted with one or more substituents selected from halogen, -CN, $-CF_3$, $-OCF_3$, $-NO_2$, $-OR^{38}$, $-NR^{38}R^{39}$ and C_{1-6}-alkyl,

wherein R^{38} and R^{39} independently are hydrogen or C_{1-6}-alkyl,

or R^{36} and R^{37} when attached to the same nitrogen atom together form a 3 to 8 membered heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulfur, and optionally containing one or two double bonds,

or R^{23} and R^{24} when attached to the same ring carbon atom or different ring carbon atoms together form a radical $-O-(CH_2)_t-CR^{40}R^{41}-(CH_2)_l-O-$, $-(CH_2)_t-CR^{40}R^{41}-(CH_2)_l-$ or $-S-(CH_2)_t-CR^{40}R^{41}-(CH_2)_l-S-$,

wherein

t and l independently are 0, 1, 2, 3, 4 or 5,

R^{40} and R^{41} independently are hydrogen or C_{1-6}-alkyl,

R^{25} to R^{30} independently are hydrogen, halogen, -CN, $-CF_3$, $-NO_2$, $-OR^{42}$, $-NR^{42}R^{43}$, C_{1-6}-alkyl, C_{3-8}-cycloalkyl or C_{4-8}-cycloalkenyl,

wherein R^{42} and R^{43} independently are hydrogen or C_{1-6}-alkyl, or

R^{42} and R^{43} when attached to the same nitrogen atom together form a 3 to 8 membered heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen and sulfur, and optionally containing one or two double bonds,

R^{31}, R^{32} and R^{33} independently are hydrogen or C_{1-6}-alkyl,

R^{34} and R^{35} independently are

- hydrogen, C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkanoyl, $-C(O)NR^{44}R^{45}$ or $-S(O)_2R^{45}$,
- aryl, aroyl, aryl-C_{1-6}-alkoxy, aryl-C_{1-6}-alkanoyl or aryl-C_{1-6}-alkyl,

  of which the aryl moieties optionally are substituted with one or more substituents selected from halogen, -CN, $-CF_3$, $-OCF_3$, $-OR^{44}$, $-NR^{44}R^{45}$ and C_{1-6}-alkyl,

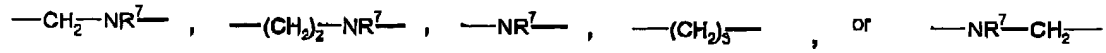
wherein R^{44} and R^{45} independently are hydrogen or C_{1-6}-alkyl, or

R^{34} and R^{35} when attached to a carbon atom together form a 3 to 8 membered cyclic ring optionally containing one or two heteroatoms selected from nitrogen, oxygen or sulfur, and optionally containing one or two double bonds, or

R^{34} and R^{35} when attached to a nitrogen atom together form a 3 to 8 membered heterocyclic ring optionally containing one or two further heteroatoms selected from nitrogen, oxygen or sulfur, and optionally containing one or two double bonds,

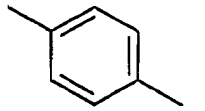
as well as any optical or geometric isomer or tautomeric form thereof or a pharmaceutically acceptable salt thereof.

5. A compound according to claim 1, wherein A is

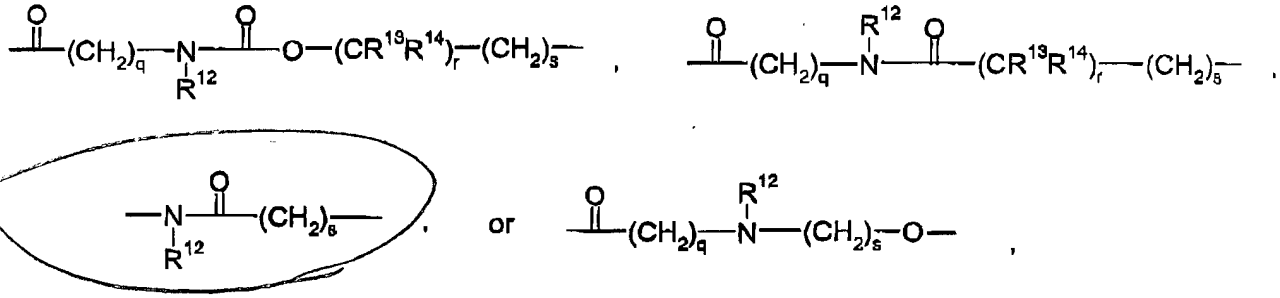


wherein R^7 is as defined in claim 1.

13. A compound according to claim 1, wherein Z is

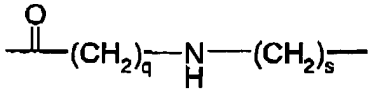


16. A compound according to claim 1, wherein X is



wherein q, r, s, R^{12}, R^{13} and R^{14} are as defined in claim 1.

17. A compound according to claim 16, wherein X is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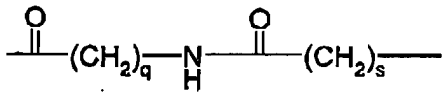
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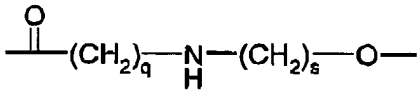
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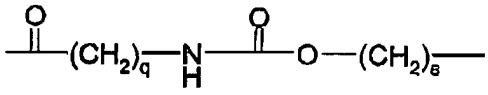
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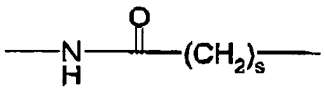
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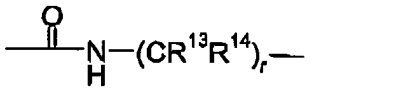
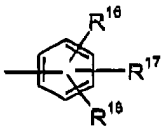

or

wherein q is 0 or 1, r is 0 or 1, s is 0, 1 or 2, and R^{13} is hydrogen or C_{1-6}-alkyl.

18. A compound according to claim 17, wherein X is -C(O)NH-, -C(O)NHCH$_2$-, -C(O)NHCH(CH$_3$)-, -C(O)NHCH$_2$CH$_2$-, or -NHC(O)-.

22. A compound according to claim 1, wherein D is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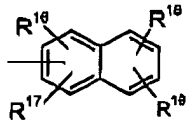
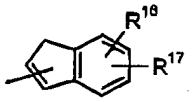
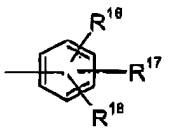
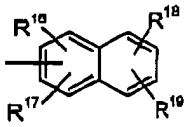

, or

,

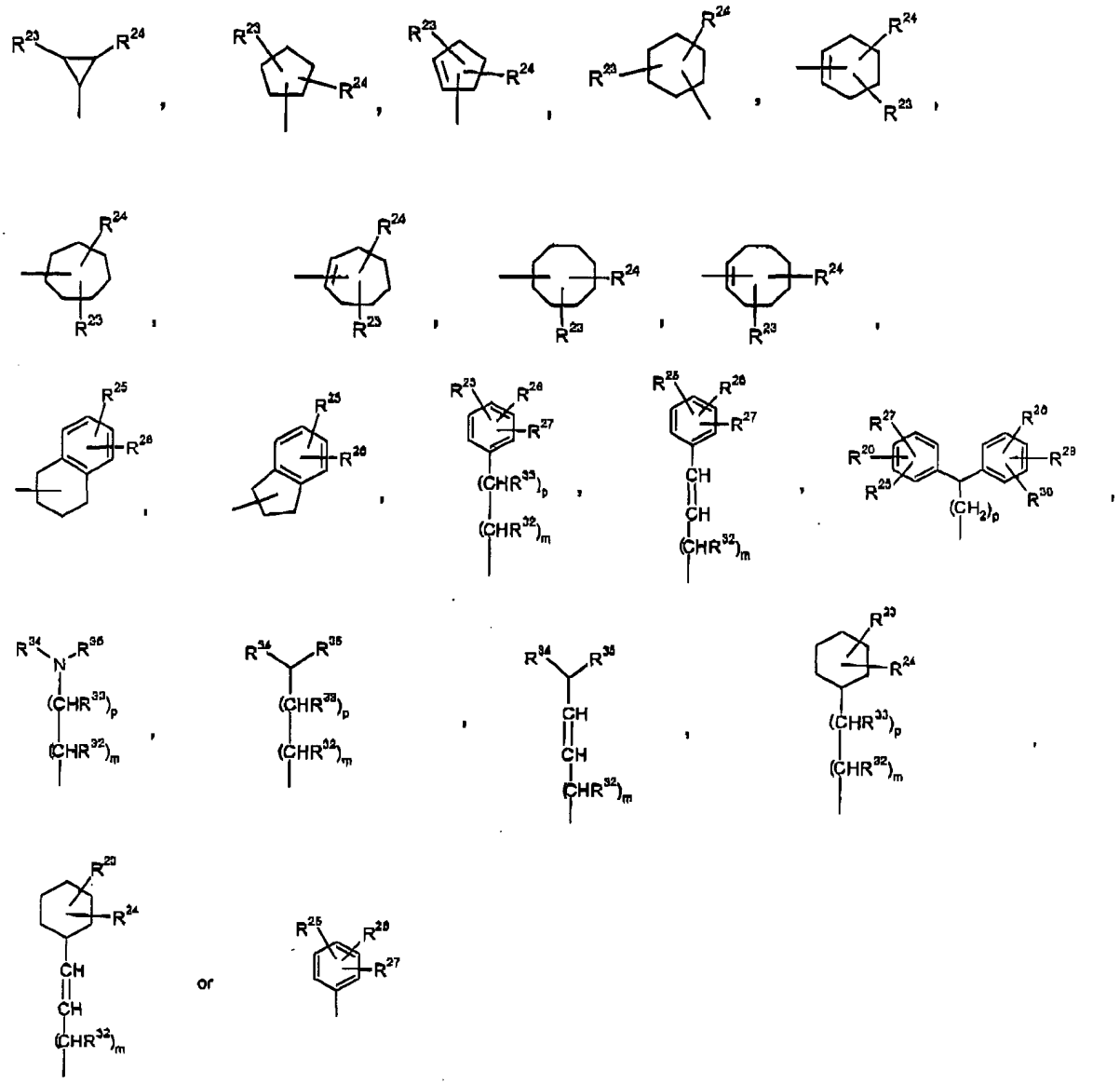
wherein R^{16}, R^{17}, R^{18}, and R^{19} are as defined in claim 1.

23. A compound according to claim 22, wherein D is


, or

,

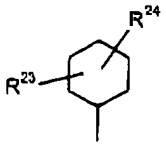
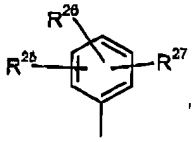
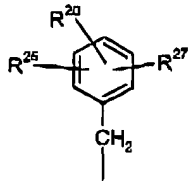
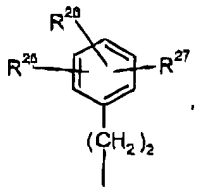
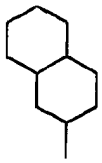
wherein R^{16}, R^{17}, R^{18} and R^{19} are as defined in claim 1.

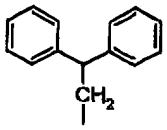
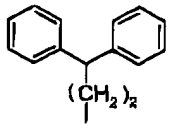
43. A compound according to claim 1, wherein E is



wherein

m, p and R^{23} to R^{30} and R^{32} to R^{35} are as defined in claim 1.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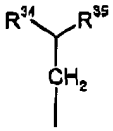
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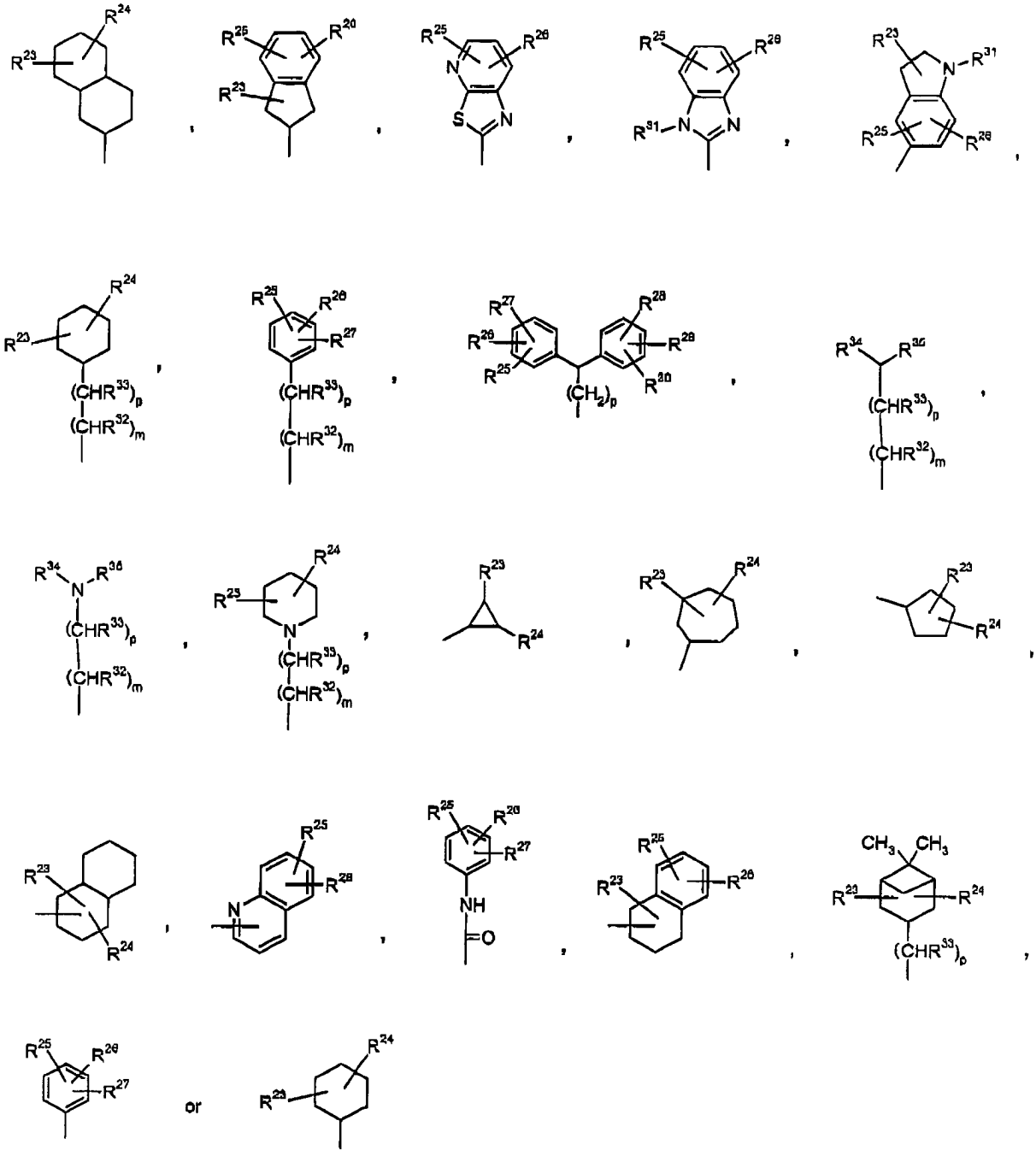
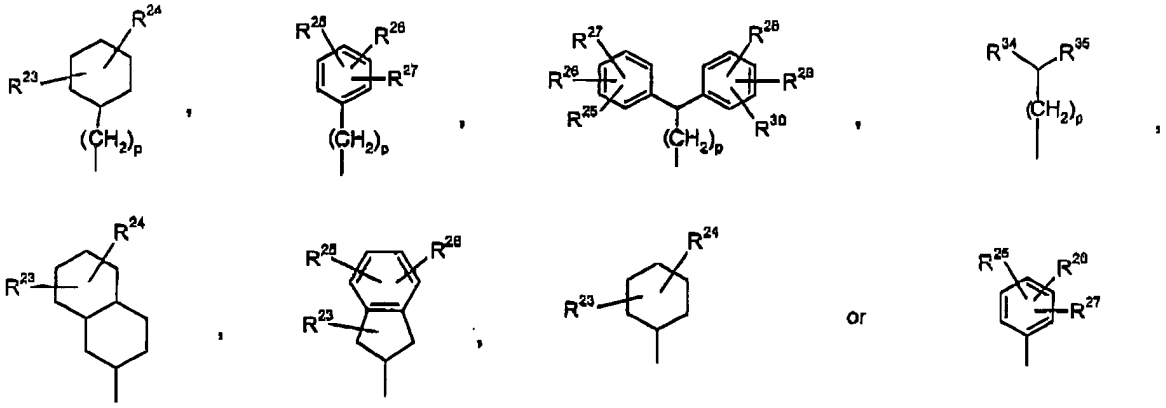
44. A compound according to claim 43, wherein E is



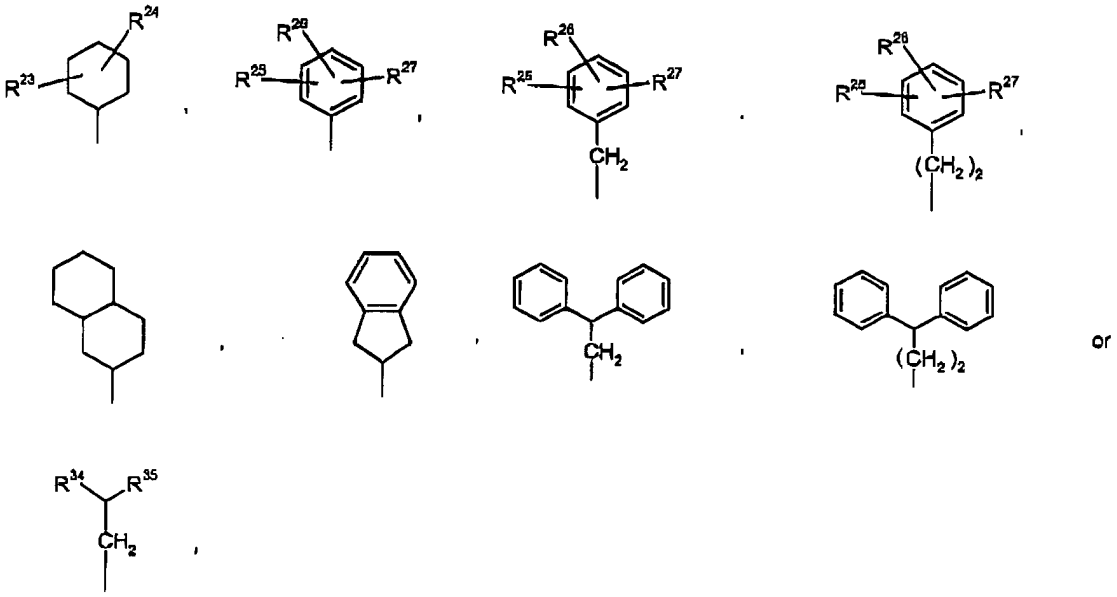
wherein m, p and R^{23} to R^{35} are as defined in claim 1.

45. A compound according to claim 44, wherein E is



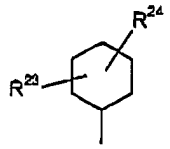
wherein p, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{34} and R^{35} are as defined in claim 1.

46. A compound according to claim 45, wherein E is



wherein R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{34} and R^{35} are as defined in claim 1.

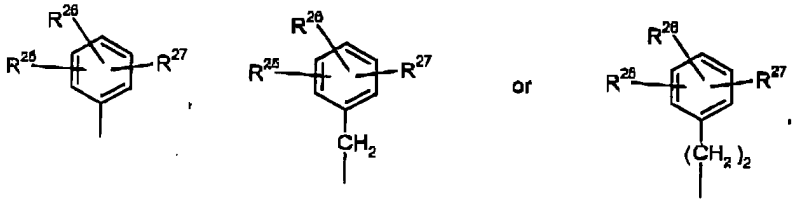
49. A compound according to claim 45, wherein E is



wherein R^{23} and R^{24} are as defined in claim 1.

51. A compound according to claim 49, wherein R^{23} and R^{24} independently are selected from hydrogen, C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkylidene, phenoxy, phenyl, $-C(O)NR^{36}R^{37}$ and $-OC(O)NH$-phenyl, of which the phenyl moiety optionally may be substituted with $-OCF_3$, wherein R^{36} and R^{37} are as defined in claim 1, or R^{23} and R^{24} together form the radical $-(CH_2)_t-CR^{40}R^{41}-(CH_2)_l-$, $-O-(CH_2)_t-CR^{40}R^{41}-(CH_2)_l-O-$, $-S-(CH_2)_t-CR^{40}R^{41}-(CH_2)_l-S-$, wherein t, l, R^{40} and R^{41} are as defined in claim 1.

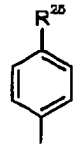
53. A compound according to claim 46, wherein E is



wherein R^{25}, R^{26} and R^{27} are as defined in claim 1.

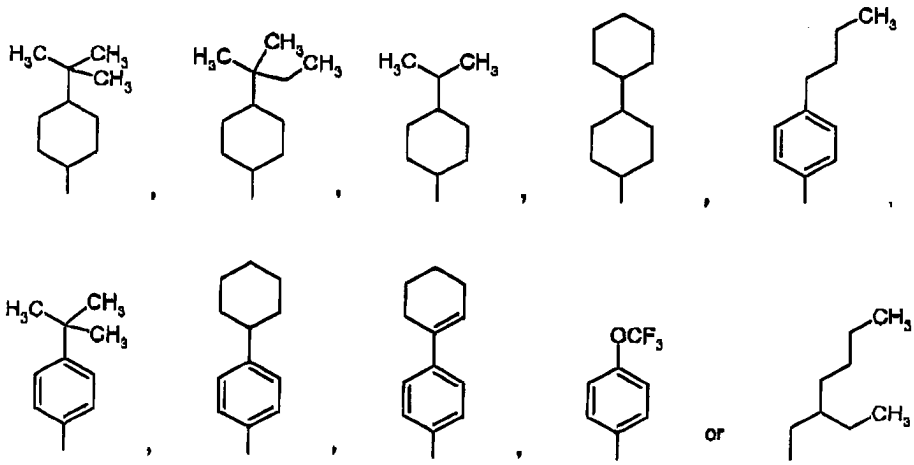
55. A compound according to claim 53, wherein R^{25}, R^{26} and R^{27} independently are selected from hydrogen, halogen, C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{3-8}-cycloalkyl, C_{4-8}-cycloalkenyl, $-CF_3$, $-OCF_3$ or $-NR^{42}R^{43}$, wherein R^{42} and R^{43} are as defined in claim 1.

56. A compound according to claim 55, wherein E is

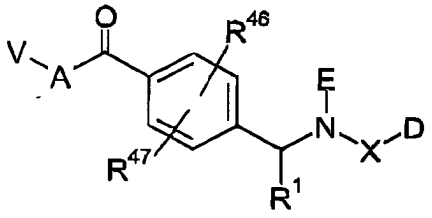


wherein R^{25} is $-OCF_3$, $-CF_3$, C_{1-6}-alkyl, piperidyl, C_{3-8}-cycloalkyl or C_{4-8}-cycloalkenyl.

57. A compound according to claim 46, wherein E is



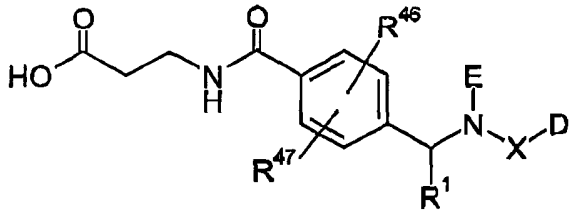
59. A compound according to claim 1 of formula (I_1):



(I_1)

wherein V, A, R^{46}, R^{47}, R^1, E, X and D are as defined in claim 1.

63. A compound according to claim 1 of formula (I_5):



(I_5)

wherein R^{46}, R^{47}, R^1, E, X and D are as defined in claim 1.

68. A compound according to claim 59, wherein R^{46} and R^{47} are both hydrogen.

69. A compound according to claim 1, which has an IC_{50} value of no greater than 5 μM as determined by a Glucagon Binding Assay (I), Glucagon Binding Assay (II) or Glucagon Binding Assay (III).

70. A compound according to claim 69 having a glucagon antagonistic activity as determined by the Glucagon Binding Assay (I), Glucagon Binding Assay (II) or Glucagon Binding Assay (III) corresponding to an IC_{50} value of less than 1 μM.

71. A compound according to claim 1, which is useful for treating Type 2 diabetes.

87. A method for treating Type 2 diabetes, said method comprising administering to a subject in need thereof an effective amount of a pharmaceutical composition of claim 89.

88. The method according to claim 87, wherein the effective amount of the compound is in the range of from about 0.05 mg to about 2000 mg.

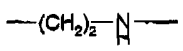
89. A pharmaceutical composition comprising, as an active ingredient, an effective amount of at least one compound of claim 1 together with one or more pharmaceutically acceptable carriers or excipients.

90. The pharmaceutical composition of claim 89 in unit dosage form, comprising from about 0.05 mg to 1000 mg of the compound.

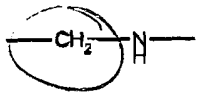
92. A method for treating hyperglycemia, said method comprising administering to a subject in need thereof an effective amount of a pharmaceutical composition of claim 89.

93. A compound according to claim 1, which is useful for treating hyperglycemia.

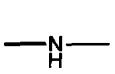
94. A compound according to claim 5, wherein A is



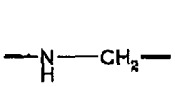
95. A compound according to claim 5, wherein A is

NO 

96. A compound according to claim 5, wherein A is

NO 

97. A compound according to claim 5, wherein A is

NO 

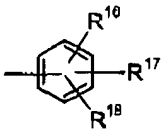
98. A compound according to claim 1, wherein R^1 is hydrogen.

NO 99. A compound according to claim 1, wherein R^1 is methyl.

100. A compound according to claim 18, wherein X is -C(O)NH-.

101. A compound according to claim 18, wherein X is -C(O)NHCH(CH_3)-.

102. A compound according to claim 23, wherein D is



wherein R^{16}, R^{17} and R^{18} are as defined in claim 1.

103. A compound according to claim 30, wherein R^{16}, R^{17} and R^{18} independently are

hydrogen, halogen, -CN, $-NO_2$, $-CF_3$, $-OCF_3$, $-SCF_3$, C_{1-6}-alkyl, C_{1-6}-alkyl substituted with hydroxy, C_{1-6}-alkyl substituted with $-S(O)_2R^{21}$, C_{1-6}-alkoxy, -S-C_{1-6}-alkyl, $-C(O)OR^{21}$, $-C(O)R^{21}$, $-CH_2(O)R^{21}$, $-C(O)NR^{21}R^{22}$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-S(O)_2CF_3$, $-S(O)_2NR^{21}R^{22}$, C_{3-8}-cycloalkyl-C_{1-6}-alkoxy, C_{3-8}-cycloalkyl-C_{1-6}-alkylthio or C_{3-8}-cycloalkylthio,

wherein R^{21} and R^{22} independently are hydrogen, C_{1-6}-alkyl, tri-C_{1-6}-alkylsilyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-6}-alkyl, phenyl or 2,3-dihydroindolyl, or R^{21} and R^{22} together with the nitrogen atom to which they are attached form a piperidine ring,

phenoxy, phenyl, benzyl, furanyl, tetrazolyl, benzoxazolyl or oxadiazolyl, of which the ring systems optionally may be substituted with halogen, $-C(O)OR^{21}$ or C_{1-6}-alkyl, wherein R^{21} is hydrogen or C_{1-6}-alkyl, or

wherein R^{16} and R^{17} in adjacent positions form the radical $-CF_2-O-CF_2-O-$ or $-O-CF_2-CF_2-O-$, and R^{18} is hydrogen.

104. A compound according to claim 103, wherein R^{16}, R^{17} and R^{18} independently are

hydrogen, halogen, -CN, $-NO_2$, $-CF_3$, $-OCF_3$, $-SCF_3$, C_{1-6}-alkyl, C_{1-6}-alkyl substituted with hydroxy, C_{1-6}-alkoxy, -S-C_{1-6}-alkyl, $-C(O)OR^{21}$, $-C(O)R^{21}$, $-CH_2(O)R^{21}$, $-C(O)NR^{21}R^{22}$, $-S(O)_2R^{21}$, $-(O)_2CF_3$ or $-S(O)_2NR^{21}R^{22}$,

wherein R^{21} and R^{22} independently are hydrogen, C_{1-6}-alkyl, tri-C_{1-6}-alkylsilyl, phenyl or 2,3-dihydroindolyl,

phenoxy, phenyl, benzyl, furanyl, tetrazolyl, benzoxazolyl or oxadiazolyl, of which the ring systems optionally may be substituted with halogen, $-C(O)OR^{21}$ or C_{1-6}-alkyl, wherein R^{21} is hydrogen or C_{1-6}-alkyl, or

wherein R^{16} and R^{17} in adjacent positions form the radical $-CF_2-O-CF_2-O-$ or $-O-CF_2-CF_2-O-$, and R^{18} is hydrogen.

105. A compound according to claim 104, wherein R^{16}, R^{17} and R^{18} independently are hydrogen, halogen, -CN, $-NO_2$, $-CF_3$, $-OCF_3$, $-SCF_3$, C_{1-6}-alkyl, C_{1-6}-alkoxy, -S-C_{1-6}-alkyl, $-C(O)OC_{1-6}$-alkyl, $-S(O)_2C_{1-6}$-alkyl, $-S(O)_2CF_3$, $-C(O)N(C_{1-6}$-alkyl)(C_{1-6}-alkyl), $-S(O)_2N$(phenyl)(C_{1-6}-alkyl), $-C(=O)C_{1-6}$-alkyl, $-CH_2OH$, $-CH_2O$(tri-C_{1-6}-alkylsilyl), 2,3-dihydroindol-1-ylsulfonyl, phenoxy, phenyl, 4-chlorophenyl, 1,3,5-trimethylbenzyl, benzoxazolyl, 2-methyltetrazol-5-yl, 2-methyl-3-methoxycarbonylfuran-5-yl or 3-isopropyl-[1,2,4]oxadiazol-5-yl).

106. A compound according to claim 30, wherein one of R^{16} to R^{18} is hydrogen.

107. A compound according to claim 30, wherein two of R^{16} to R^{18} are hydrogen.

108. A compound according to claim 30, wherein R^{16} and R^{17} are both hydrogen and R^{18} is $-OCF_3$, $-SCF_3$ $-CF_3$, $-S(O)_2CH_3$, phenyl, halogen, C_{1-6}-alkyl, nitro, -S-C_{1-6}-alkyl or $-S(O)_2NR^{21}R^{22}$, wherein R^{21} is C_{1-6}-alkyl and R^{22} is phenyl.

109. A compound according to claim 30, wherein R^{16} and R^{17} are both hydrogen and R^{18} is $-OCF_3$ or halogen.

110. A compound according to claim 30, wherein R^{16} is hydrogen and R^{17} and R^{18} are both halogen or are both $-CF_3$.

111. A compound according to claim 30, wherein R^{16} is hydrogen, R^{17} is $-CF_3$ and R^{18} is halogen, -CN, C_{1-6}-alkoxy or $-OCF_3$.

112. A compound according to claim 30, wherein R^{16} is hydrogen, R^{17} is $-OCF_3$ and R^{18} is $-S(O)_2CH_3$, $-CH_2O$-tri-C_{1-6}-alkylsilyl, benzoxazolyl or $-CH_2OH$.

113. A compound according to claim 30, wherein R^{16} is hydrogen, R^{17} is C_{1-6}-alkyl and R^{18} is $-S(O)_2NR^{21}R^{22}$, wherein R^{21} is C_{1-6}-alkyl and R^{22} is phenyl.

114. A compound according to claim 30, wherein R^{16}, R^{17} and R^{18} are selected from hydrogen, $-OCF_3$, $-CF_3$, -Br, -F and -Cl.

115. A method for treating impaired glucose tolerance, said method comprising administering to a subject in need thereof an effective amount of a pharmaceutical composition of claim 89.

116. A compound according to claim 1, which is useful for treating impaired glucose tolerance.

117. A method for treating obesity, said method comprising administering to a subject in need thereof an effective amount of a pharmaceutical composition of claim 89.

118. A compound according to claim 1, which is useful for treating obesity.

Attorney Docket No.: 5576.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Lau et al.

Application No.: 09/572,553 Group Art Unit: 1624

Filed: May 16, 2000 Examiner: S. Patel

Confirmation No: 5348

For: Glucagon Antagonists/Inverse Agonists

AMENDMENT UNDER 37 C.F.R. 1.312

Commissioner for Patents
Arlington, VA 22202-3513
Attn: Box Issue Fee

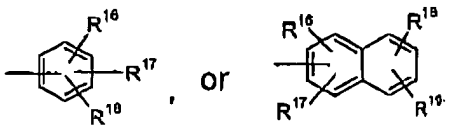
Sir:

This Amendment is submitted in response to a May 23, 2002 Notice of Allowance and is made because each of allowed claims 23, 44, 45, 46, 49, 51, 53, 55 and 102 were in improper form as they depended both on claim 1 and on another claim.

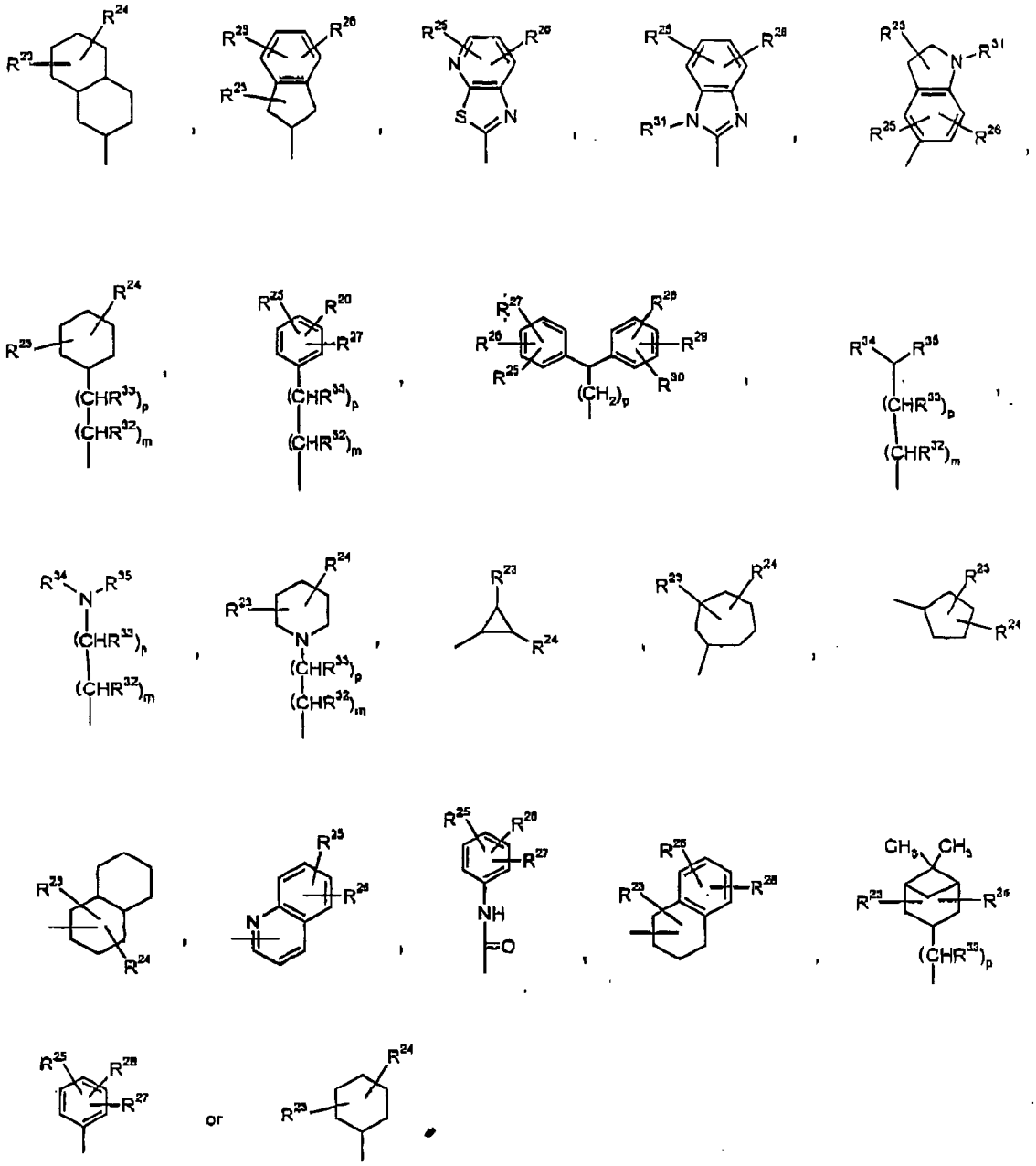
IN THE CLAIMS:

Please amend the following claims:

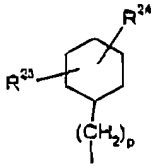
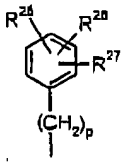
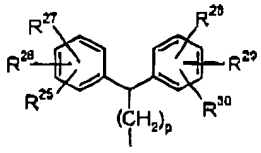
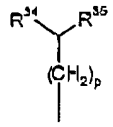
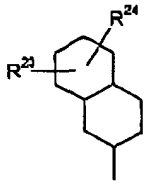
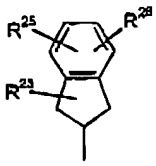
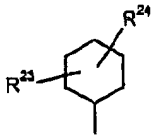
23. (Twice Amended) A compound according to claim 22, wherein D is



44. (Amended) A compound according to claim 43, wherein E is



45. (Amended) A compound according to claim 44, wherein E is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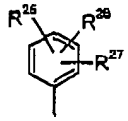
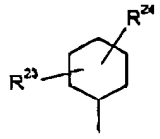
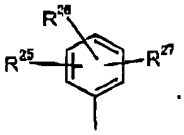
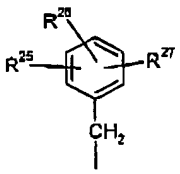
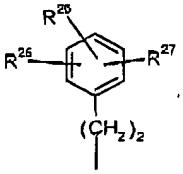
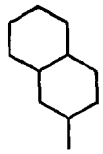
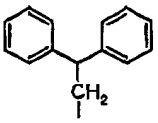
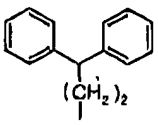
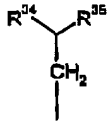
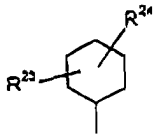


46. (Amended) A compound according to claim 45, wherein E is

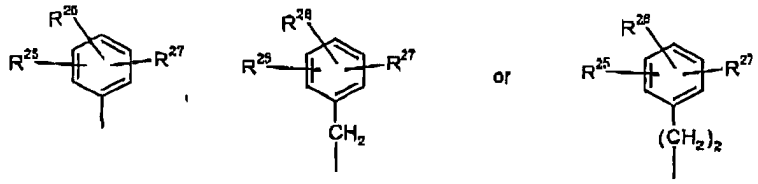


or


49. (Amended) A compound according to claim 45, wherein E is



51. (Amended) A compound according to claim 49, wherein R^{23} and R^{24} independently are selected from hydrogen, C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkylidene, phenoxy, phenyl, -C(O)$NR^{36}R^{37}$ and -OC(O)NH-phenyl, of which the phenyl moiety optionally may be substituted with $-OCF_3$, or R^{23} and R^{24} together form the radical $-(CH_2)_t-CR^{40}R^{41}-(CH_2)_t-$, $-O-(CH_2)_t-CR^{40}R^{41}-(CH_2)_t-O-$, $-S-(CH_2)_t-CR^{40}R^{41}-(CH_2)_t-S-$.

53. (Amended) A compound according to claim 46, wherein E is



55. (Amended) A compound according to claim 53, wherein R^{25}, R^{26} and R^{27} independently are selected from hydrogen, halogen, C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{3-8}-cycloalkyl, C_{4-8}-cycloalkenyl, $-CF_3$, $-OCF_3$ or $-NR^{42}R^{43}$.

102. (Amended) A compound according to claim 23, wherein D is